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Geriatric Oncology

High Serum Vitamin B12 Levels Associated with C-Reactive Protein in Older Patients with Cancer

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. High serum vitamin B12 levels • C-reactive protein • Early death • Unplanned hospitalization • Older patients with cancer

Abstract

Background. A Comprehensive Geriatric Assessment (CGA) has been proposed to assess prognosis and to adapt oncological care in older patients with cancer. However, few biological markers are incorporated in the CGA.

Methods. This comparative study on older patients with cancer was realized before final therapeutic decision and during a CGA that included biological markers. Our objective study was to know if the serum vitamin B12–C-reactive protein index (BCI) can help to estimate early death and unplanned hospitalization. Associations between BCI and unplanned hospitalization or mortality were analyzed using ordered multivariate logistic regression.

Findings. We included 621 older cancer adults in outpatient care with a median age of 81 years (range, 70–98 years) from September 2015 to May 2018. In this study, 5.6% of patients died within 3 months, 8.8% had unplanned hospitalization within 1 month, and 11.4% had unplanned hospitalization within 3 months. Hypercobalaminemia was present in 83 patients (13.4%), and 34 patients (5.5%) had BCI >40,000. According to the multivariate analysis, BCI was a prognostic factor of mortality within 3 months and unplanned hospitalizations at 1 and 3 months. Impaired activities of daily living (ADL) and palliative care were also risk factors for mortality within 3 months. Impaired instrumental ADL, low albumin level, and palliative care were risk factors for unplanned hospitalization at 1 month.

Interpretation. BCI could be routinely added to the CGA process, as part of a pretreatment workup, in order to assess more precisely the frailties and to adapt oncological care in older patients treated for cancer. ***The Oncologist*** 2020;25:e1980–e1989

Implications for Practice: Aging comes with an increase of frailties and comorbidities. To identify frailties in older patients with cancer, this study used a Comprehensive Geriatric Assessment, which allowed for the adaptation of each treatment plan in accordance with the individual needs of the patients. However, biological characteristics were not included in this assessment. This study showed that hypercobalaminemia and vitamin B12 -C-reactive protein index may be potential markers for cancer with poor prognosis, particularly in the older population. These biological markers can be used in geriatric oncology and general medicine.

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Introduction

Older persons make up a large percentage of the cancer population. Currently, cancer affects nearly 60% of people aged ≥65 years in Europe and nearly 50% of people aged >65 years in the U.S. [1, 2]. For many years, older patients with cancer have been treated according to their physiological age regardless of their state of health. The development of geriatric oncology has greatly improved the management of these older patients, with a Comprehensive Geriatric Assessment (CGA) being conducted before and during cancer treatment on older patients with cancer who are identified as frail according to the G8 screening tool [3–5]. CGA assesses geriatric frailties and syndromes to improve oncological treatment outcomes in older patients and to propose a personalized care plan. But biological characteristics are not included in this CGA.

Yet, Carmel et al. in 1977 reported a significant association between high serum vitamin B12 levels, or hypercobalaminemia (HCbl), and solid tumors. HCbl in solid tumors is related to an excess synthesis of transcobalamins by the tumor or an increase in haptocorrin secondary to hyperleukocytosis [6–8]. In the same way, HCbl may also be a potential marker for cancer with poor prognosis, in particular in the geriatric population [9, 10]. Likewise, the vitamin B12–C-reactive protein index (BCI) has been proposed as a prognostic indicator in patients with metastatic cancer [9]. In the study by Kelly et al., an elevated BCI (>40,000) predicts poor survival in patients with advanced cancer with a median survival of 29 days [11].

To determine whether BCI would be an interesting biological marker in terms of survival and unplanned hospitalization in patients aged ≥70 years with cancer, we conducted a comparative study in older patients referred for CGA prior to oncological treatment.

Materials and Methods

Population Description

This comparative study was conducted at Marseille University Hospital in France from September 2015 to May 2018 on 621 patients aged ≥70 years. Patients were referred from the oncology and surgery units to perform a CGA before initiation of any oncological treatment. This CGA was realized in the Geriatric Day Hospital, and the included patients were assessed in outpatient care.

Ethics

This study was approved by the ethics committee. All the patients were registered at baseline in compliance with the French database and privacy law (Commission Nationale de l'Informatique et Liberté registration number: 2017-33).

Clinical and Laboratory Data

Oncological, geriatric, and biological data were collected prospectively, but thereafter, the final oncological treatment administered by the clinicians, overall survival (OS), and unplanned hospitalizations were recorded retrospectively. Patients who had received vitamin B12 supplementation in the weeks preceding CGA and patients who were hospitalized during the CGA time were excluded from the study.

For each patient, the following data were collected during the CGA:

a. Demographics (age, sex), lifestyle (home vs. follow-up and rehabilitation care vs. nursing home), tumor site (solid vs. hematological malignancy), extension of the tumor (localized or advanced disease), treatment strategy (active vs. palliative) decided by oncologists after CGA, and concordance between anticipated treatment strategy before CGA and treatment decision after CGA.
b. Functional status determined using activities of daily living (ADL) according to Katz et al. and instrumental ADL (IADL) according to Lawton et al.; mobility determined using the Timed Up and Go test (TUG), the unipodal test, gait speed, and whether patients had had a fall in the 3 months preceding the CGA; and nutritional status using weight, body mass index (BMI), and Mini Nutritional Assessment (MNA). In addition, we collected performance status (PS) and ONCODAGE (G8) [5, 12–18].
c. Laboratory data: hemoglobin (Hb), albumin level, vitamin B12, C-reactive protein (CRP), and BCI, which is the product of multiplying the CRP level with the vitamin B12 level (B12 × CRP).
d. Evolution: OS, unplanned hospitalization.

The validated cutoffs for scales as recommended and for laboratory data are specified in Table 1.

Statistical Analysis

OS is the time between the diagnosis of the disease and death whatever the cause. Patients who were alive and relapsed at the end of the follow-up were censored. All quantitative variables are presented using descriptive statistics: number of subjects and average. Qualitative variables are described by absolute frequencies and percentages (proportion). Variables with $p < .05$ were considered significant. The log-rank test and univariate Cox models were used for comparisons of survival. Variables significant in univariate analysis with a significance $p < .2$ were considered as eligible to be included in the multivariate Cox model. However, for the survival model, as the number of events was low (32 deaths), we did not enter simultaneously in the multivariate Cox model all the variables significant in univariate analysis. We decided to keep in the final model only three of the significant variables, choosing those that had the least missing data. The same procedure was chosen for the multivariate logistic regressions on unplanned hospitalizations (within 1 or 3 months), with a total number of four significant variables in the final models (number of events = 52 and 66, respectively). For the three multivariate models, adjustment on age was tested (although age was not significant in univariate analysis) but was not kept as it did not improve the models. Statistical analyses were performed with SPSS Software for Windows version 17.0.

Table 1. Patient demographics and clinical and geriatric characteristics (n = 621)

Characteristics	Patients n (%)
Sex ratio	
Women	241 (38.8)
Men	380 (61.2)
Age (median: 81 years)	
70–75 years	92 (14.8)
75–85 years	379 (61)
>85 years	150 (24.2)
Lifestyle	
Home	553 (89.0)
Nursing home	31 (5.0)
Follow-up and rehabilitation unit	37 (6.0)
ADL	
6	390 (62.8)
<6	231 (37.2)
IADL	
<4	322 (51.8)
4	298 (48.0)
Missing	1 (0.2)
BMI	
<18	27 (4.4)
18–21	85 (13.7)
21	506 (81.5)
Missing	3 (0.4)
Tumor type	
Solid	585 (94.0)
Hematological malignancy	36 (5.8)
Missing	1 (0.2)
Metastatic stage[a]	
No	349 (59.7)
Yes	205 (35.0)
Missing	31 (5.3)
Anticipated treatment strategy	
Active	568 (91.5)
Palliative	34 (5.5)
Missing	19 (3.0)
Treatment	
In concordance with CGA	504 (81.2)
Not in concordance	98 (15.8)
Missing	19 (3.0)
MNA	
<17	74 (12.0)
17–23.5	255 (41.0)
>23.5	260 (41.9)
Missing	32 (5.1)
TUG	
<20 s	205 (33.0)
≥20 s	394 (63.5)
Missing	22 (3.5)
Unipodal test	
<5 s	400 (64.4)
≥5 s	105 (16.9)
Missing	116 (18.7)
Gait speed	
≥0.8 m/s	381 (61.4)
<0.8 m/s	168 (27.1)
Missing	72 (11.5)
Hb	
Hb ≥10 g/dL	546 (87.9)
Hb <10 g/dL	74 (11.9)
Missing	1 (0.2)
HCbl	
≤569 pmol/L	537 (86.4)
>569 pmol/L	83 (13.4)
Missing	1 (0.2)
BCI	
>40,000	34 (5.5)
≤40,000	582 (93.7)
Missing	5 (0.8)
PS	
<2	426 (68.5)
≥2	138 (22.2)
Missing	58 (9.3)
G8	
≤14/17	425 (68.5)
>14/17	94 (15.1)
Missing	102 (16.4)
Albumin	
<30	17 (2.7)
30–35	65 (10.5)
>35	528 (85.2)
Missing	10 (1.6)
Fall within 3 months	
No	508 (81.8)
Yes	112 (18.0)
Missing	1 (0)

[a]n = 585 solid tumors.

Abbreviations: ADL, activities of daily living; BCI, B12 × C-reactive protein index; BMI, body mass index; CGA, Comprehensive Graphic Assessment; Hb, hemoglobin; HCbl, hypercobalaminemia; IADL, instrumental activities of daily living; MNA, Mini Nutritional Assessment; PS, performance status; TUG, Timed Up and Go test.

Results

Patient Characteristics and CGA

In our study, 621 patients were recruited. The median age was 81 years (range, 70–98 years), and 61% were men. HCbl was present in 83 patients (13.4%), and 34 patients

Table 2. Type of tumors

Tumor	Type	Patients (n = 621), n (%)
Lung (excluding mesothelium)	Solid tumor	142 (23)
Prostate cancer	Solid tumor	134 (22)
Gastrointestinal tract	Solid tumor	79 (13.2)
Breast cancer	Solid tumor	59 (10)
Basal cell and squamous cell carcinoma	Solid tumor	28 (5)
Kidney cancer	Solid tumor	25 (4)
Head and neck cancer	Solid tumor	24 (3.9)
Myeloma	Hematological malignancy	15 (2.4)
Urothelial tumor	Solid tumor	14 (2.3)
Ovary cancer	Solid tumor	13 (2)
Diffuse large B-cell lymphoma	Hematological malignancy	12 (2)
Cervical cancer	Solid tumor	11 (1.8)
Endometrial cancer	Solid tumor	10 (1.6)
Hepatocellular carcinoma	Solid tumor	10 (1.6)
Pancreas	Solid tumor	9 (1.4)
Thyroid cancer	Solid tumor	8 (1.3)
Melanoma	Solid tumor	7 (1.1)
Bile duct carcinoma	Solid tumor	6 (1)
Mesothelium	Solid tumor	5 (0.8)
T-cell lymphoma	Hematological malignancy	5 (0.8)
Chronic lymphoid leukemia	Hematological malignancy	2 (0.3)
Acute myeloid leukemia	Hematological malignancy	1 (0.1)
Chronic myeloid leukemia	Hematological malignancy	1 (0.1)
Other tumor	Solid tumor	1 (0.1)

(5.5%) had BCI >40,000. The majority of tumors were solid (94.2% of patients), in particular, lung cancer in 23% of patients, prostate cancer in 22%, gastrointestinal tract cancer in 13.2%, and breast cancer in 10%; 205 (35%) patients had metastatic cancer. All types of tumor are detailed in Table 2. The majority of patients (81.2%) received the treatment chosen by clinicians after CGA.

Patient demographics, as well as the clinical and geriatric characteristics, are presented in Table 1.

In our study, 32 patients (5.6%) died within 3 months; no survival data were available for 51 patients (data for these patients were censored at the last known date they were alive). Of early deaths, 19 (59.4%) were attributable to cancer progression, 5 (15.6%) to treatment-related complications (cardiac decompensation on grade 3 anemia, septic shock on postchemotherapy grade 4 neutropenia, nosocomial infection on pleural drainage, and two preoperative surgical complications), 5 (15.6%) to other reasons (two gastrointestinal bleedings, cerebral hemorrhage, cerebral thrombophlebitis, fall with cranial trauma), and the last 3 (9.4%) to unknown reasons. Fifty-two patients (8.8%) had unplanned hospitalization within 1 month; no data were available for 29 patients. Sixty-six patients (11.4%) had unplanned hospitalization within 3 months; no data were available for 40 patients. The median follow-up time was 10 months (range, 1–35 months).

Early Death Within 3 Months

Univariate and multivariate Cox models for 3-month survival are presented in Table 3.

In univariate analysis, the risk of 3-month mortality was significantly higher in patients with palliative treatment, impaired geriatric factors (ADL, TUG, MNA, unipodal test, gait speed, and BMI), anemia, HCbl, and BCI >40,000. In the multivariate Cox model, palliative treatment (hazard ratio [HR], 4.6; 95% confidence interval [CI], 1.9–11.0), impaired ADL (HR, 2.5; 95% CI, 1.14–5.53), and BCI (HR, 6.39; 95% CI, 2.68–15.4) remained significantly associated with the outcome.

Another multivariate model (not shown) using HCbl instead of BCI had comparable results, with palliative treatment and impaired ADL remaining significantly associated with the 3-month mortality risk.

Unplanned Hospitalization Within 1 Month

After logistic regression, the following factors remained independently associated with a 1-month unplanned hospitalization risk: palliative care (vs. active treatment) (odds ratio [OR], 2.77; 95% CI, 1.03–6.88), BCI >40,000 (OR, 3.31; 95% CI, 1.26–8.32), albumin level <35 g/L (OR, 1.87; 95% CI, 1.04–3.24), and IADL (OR, 2.06; 95% CI, 1.05–4.23) (Table 4).

Unplanned Hospitalization Within 3 Months

After logistic regression, the following factors remained independently associated with a 3-month unplanned hospitalization risk: BCI >40,000 (OR, 5.12; 95% CI, 2.20–12.27) and albumin level <35 g/L (OR, 1.71; 95% CI, 0.98–2.89) (Table 5).

Discussion

In outpatient care for older patients with cancer, identifying factors associated with a higher risk of early death or unplanned hospitalizations are essential in determining the risk profile of each patient. Establishing prognostic factors in this older population with cancer is all the more useful because advanced age has been identified as predictive of mortality and the rate of unplanned hospitalizations is higher in older adults than young adults [19, 20]. To our knowledge, this is the first study to show that BCI is a marker for higher rates of unplanned hospitalization in older patients with cancer. In accordance with the literature, our study confirms the link between BCI and mortality in this same population.

The association between HCbl and solid neoplasms has been described in a few studies [6, 21, 22]. Furthermore, HCbl is an anomaly frequently observed in hematological malignancies [8, 21]. HCbl predicts early death in the cancer

Table 3. Factors associated with a 3-month mortality risk in older patients with cancer (Cox model)

	Univariate			Multivariate (n = 535)		
Variables	**Alive (n = 538), n (%)[a]**	**Died (n = 32), n (%)[a]**	**p value**	**Coefficient**	**HR (95% CI)**	**p value**
Age						
70–75 years	82 (15.2)	4 (12.5)				
75–85 years	324 (60.3)	19 (59.4)				
>85 years	132 (24.5)	9 (28.1)	.63			
Metastatic stage[b]						
Yes	178 (35.5)	15 (51.7)				
No	324 (64.5)	14 (48.3)	.07			
BMI						
<18	20 (3.7)	2 (6.3)				
18–21	66 (12.3)	12 (37.5)	**<.0001**			
>21	450 (83.6)	18 (56.3)				
Palliative treatment						
Yes	22 (4.1)	7 (21.9)		1.5	4.6 (1.9–11.0)	**.006**
No	499 (92.8)	24 (75)	<.0001		1	
ADL						
<6	187 (34.8)	19 (59.4)	**.004**	0.9	2.5 (1.14–5.53)	**.02**
6	349 (64.9)	12 (37.5)			1	
MNA[b]						
<17	60 (11.2)	8 (25)				
17–23.5	218 (40.5)	12 (37.5)	**.003**			
<23.5	241 (44.8)	6 (18.8)				
TUG[b]						
<20 s	360 (66.9)	12 (37.5)	**.004**			
≥20 s	165 (30.6)	17 (53.1)				
Unipodal test[b]						
<5 s	374 (69.5)	26(81.3)	**.005**			
≥5 s	104 (19.3)	1 (3.1)				
Gait speed[b]						
≥0.8 m/s	342 (63.6)	11 (34.3)				
<0.8 m/s	135 (25.1)	16 (50)	**.001**			
Hb						
≥10 d/dL	483 (89.8)	22 (68.8)				
<10 d/dL	54 (10.1)	10 (31.3)	**.0006**			
HCbl						
≤569 pmol/L	478 (88.8)	19 (59.4)				
>569 pmol/L	60 (11.2)	13 (40.6)	**<.0001**			
BCI						
>40,000	21 (3.9)	8 (25)	**<.0001**	1.85	6.39 (2.68–15.4)	**<.0001**
≤40,000	513 (95.4)	24 (75)			1	

[a]Total percentages do not always reach 100% because of missing data.
[b]Metastatic stage: n = 554 patients; Unipodal test: n = 505 patients; Gait speed: n = 504 patients; TUG: n = 599 patients; MNA: n = 589 patients. For all other variables, missing values <5%.
Abbreviations: ADL, activities of daily living; BCI, B12 × C-reactive protein index; BMI, body mass index; CI, confidence interval; Hb, hemoglobin; HCbl, hypercobalaminemia; HR, hazard ratio; MNA, Mini Nutritional Assessment; TUG, Timed Up and Go test.

population and in hospitalized older patients [10, 23–25]. Of the 621 patients included in our study, 13.4% had HCbl, whereas in the study by Zulfiqar et al. on 190 patients hospitalized in an acute geriatric unit, 25.3% had HCb1 [25]. Patients ≥75 years of age were more likely to have HCbl (p = .0416). In another similar study by Salles et al. on 488 older outpatients, 33.8% had HCbl, whereas in the study by Tal et al. on 1,570 patients with a mean age of

Table 4. Factors associated with a 1-month unplanned hospitalization risk in older patients with cancer (logistic regression)

	Univariate			Multivariate (*n* = 559)	
Variables	**Unplanned hospitalization (*n* = 52), *n* (%)[a]**	**No unplanned hospitalization (*n* = 540), *n* (%)[a]**	***p* value**	**OR (95% CI)**	***p* value**
Age					
70–75 years	7 (13.5)	80 (14.8)			
75–85 years	32 (61.5)	329 (60.9)			
>85 years	13 (25.0)	131 (24.6)	0.96		
Metastatic stage[b]					
Yes	25 (48.1)	180 (33.3)			
No	22 (42.3)	327 (60.5)	**.002**		
Palliative treatment					
Yes	9 (17.3)	22 (4.1)		2.77 (1.03–6.88)	**.03**
No	41 (78.8)	502 (93)	**.0002**	1	
ADL					
<6	27 (51.9)	189 (35)	**.02**		
6	25 (48.1)	349 (64.6)			
IADL					
<4	38 (73.1)	268 (49.6)	**.002**	2.06 (1.05–4.23)	**.04**
4	14 (26.9)	272 (50.4)		1	
MNA[b]					
<17	12 (23.1)	57 (10.6)			
17–23.5	27 (51.9)	218 (40.4)	**.0006**		
>23.5	11 (21.2)	239 (44.3)			
Malnutrition					
Yes	32 (61.5)	189 (35)	**.0001**		
No	18 (34.6)	347 (64.3)			
TUG[b]					
<20 s	23 (44.2)	357 (66.1)	**.02**		
≥20 s	23 (44.2)	171 (31.7)			
Fall within 3 months					
No	34 (65.4)	453 (83.9)			
Yes	18 (34.6)	86 (15.9)	**.001**		
Hb					
≥10 g/dL	38 (73.1)	483 (89.4)			
<10 g/dL	14 (26.9)	56 (10.4)	**.0008**		
HCbl					
≤569 pmol/L	36 (69.2)	476 (88.1)			
>569 pmol/L	16 (30.8)	64 (11.9)	**.0003**		
BCI					
>40,000	12 (23.1)	21 (3.9)	**<.0001**	3.31 (1.26–8.32)	**.01**
≤40,000	40 (76.9)	514 (95.2)		1	
Albumin					
30–35 g/L	21 (39.4)	56 (10.6)	**<.0001**	1.87 (1.04–3.24)	**.03**
>35 g/L	31 (59.6)	472 (87.4)		1	
G8[b]					
≤14	39 (75)	372 (68.9)	**.04**		
>14	2 (3.8)	89 (16.5)			

(continued)

Table 4. (continued)

Variables	Univariate			Multivariate (n = 559)	
	Unplanned hospitalization (n = 52), n (%)[a]	No unplanned hospitalization (n = 540), n (%)[a]	p value	OR (95% CI)	p value
PS[b]					
<2	25 (48.1)	387 (71.7)			
≥2	20 (38.5)	111 (20.6)	**.001**		

[a]Total percentages do not always reach 100% because of missing data.
[b]Metastatic stage: n = 554; patients; G8: n = 502 patients; PS: n = 543 patients; TUG: n = 599; MNA: n = 589. For all other variables, missing values <5%.
Abbreviations: ADL, activities of daily living; BCI, B12 × C-reactive protein index; CI, confidence interval; Hb, hemoglobin; HCbl, hypercobalaminemia; IADL, instrumental activities of daily living; MNA, Mini Nutritional Assessment; OR, odds ratio; PS, performance status; TUG, Timed Up and Go test.

81 years, 50% had HCbl [10, 24]. The frequency of HCbl in our study was similar to that observed by Chiche et al.; 18.5% of patients in the internal medicine unit with a mean age of 77 years had HCbl, and 23% of patients in the study had cancer [21]. Likewise, in the study by Jammal et al. on 3,702 hospitalized patients, 12% had HCbl [26]. These differences in the prevalence of HCbl can be explained by the fact that the inclusion criteria were different (geriatric population or cancer population) and that laboratory standards for serum vitamin B12 levels vary from one hospital to another.

Geissbülher et al. recently tested the BCI. In this study on 161 older patients with a median age of 76 years, an elevated BCI (>40,000) was associated with a 3-month mortality of 90% in patients with advanced cancer [9]. Kelly and coworkers predicted an elevated BCI (>40,000) as a factor of poor prognosis in 329 older patients with advanced and metastatic cancer (p < .01) [11]. In our study, only 5.5% of patients had a BCI >40,000 versus 38.9% in the study by Kelly et al. because our metastatic cancer rate was lower than in the studies by Geissbülher et al. and Kelly et al. [9, 11]. Using multivariate analysis in our study, BCI (p < .0001) was prognostic factor of 3-month mortality. These results were similar to those of the studies described previously [9, 11].

Concerning prognostic factors for unplanned hospitalizations within 1 and 3 months, our work is innovative. In the oncological literature, there are little data on factors influencing early hospitalizations in older patients with cancer [27, 28]. Multivariate analysis showed that BCI >40,000 persisted as a prognostic factor for unplanned hospitalizations within 1 and 3 months (p = .01 and p = .0002, respectively). In fact, BCI factor predicts poor survival and the risk of unplanned hospitalization in older ambulatory patients with cancer.

In our study, geriatric disabilities and several screening tools for vulnerability were selected as survival prognostic and unplanned hospitalization factors. Functional status impairment according to ADL was statistically significant for 3-month OS (p = .02), and IADL was statistically significant for unplanned hospitalizations within 1 month (p = .04). Loss of functional capacity could increase the risk of treatment-related complications and the risk of poor outcomes in older patients with cancer [29]. Functional capacities concern mobility disorders, cognitive impairment, depression, and sensorial disorders. ADL score was associated with OS in other studies about older patients with cancer [30, 31], and IADL score was independently associated with unplanned hospitalizations of patients with ovarian cancer [31]. Consequently, functional capacities are an essential part of the CGA in order to organize home care to ensure the good progress of the oncological treatment and to avoid hospitalizations [4]. Some studies have shown the impact of IADL on survival of older patients with cancer [31, 32], and IADL is included in the Chemotherapy Risk Assessment Scale for High Age (CRASH) chemotoxicity score [33]. Nutritional status is also very important for survival of older patients with cancer and the risk of treatment complications. In our work, albumin level < 35 g/L was an unplanned hospitalization risk factor within 1 and 3 months (p = .03 and p = .05, respectively). In the literature, low albumin level was associated with overall survival in solid tumors and hematological malignancies [31, 34] but not with hospitalizations of older patients with cancer.

Age and, in particular, age groups (70–75 years, 75–85 years, and >85 years) have no influence on OS and unplanned hospitalization risk in our work. In the literature, the influence of age on outcomes of older patients with cancer is controversial, in particular in the "oldest-old" subgroup (>85 years). In the chemotoxicity scores Cancer and Aging Research Group (CARG) and CRASH, age was included only in the CARG score [33, 35]. In a recent predicting death score in older adults with colon cancer, age >82 years was selected as prognostic factor [36]. But older age alone should not be decisive for oncological treatment decision making; patient decisions and high-risk factors such as functional status (IADL or ADL), malnutrition, and cognitive or mobility impairment are more important [37].

We recommend that BCI be determined routinely before initiation of oncological treatment in older patients with cancer because it is a prognostic factor of early death, and CRASH score or the score for assessing the risk of chemotoxicity in older patients could be proposed in this population [33, 35]. BCI would be a risk factor in this early hospitalization scoring system.

This study also has some limitations, as it was monocentric. Survival and unplanned hospitalization rates were calculated after CGA and not after initiation of oncological treatment, but some patients had been hospitalized or died

Table 5. Factors associated with a 3-month unplanned hospitalization risk in older patients with cancer (logistic regression)

	Univariate			Multivariate (n = 548)	
Variables	**Unplanned hospitalization (n = 66), n (%)[a]**	**No unplanned hospitalization (n = 515), n (%)[a]**	**p value**	**OR (95% CI)**	**p value**
Age					
70–75 years	9 (13.6)	79 (15.3)			
75–85 years	42 (63.7)	310 (60.2)			
>85 years	15 (22.7)	126 (24.5)	.86		
Metastatic stage[b]					
Yes	29 (43.9)	173 (33.6)	.15		
No	35 (53.0)	306 (59.4)			
Palliative treatment					
Yes	6 (9.0)	22 (4.2)	.15	1.36 (0.43–3.73)	.54
No	57 (86.3)	478 (92.8)		1	
Lifestyle					
Home	51 (77.3)	468 (90.9)			
Follow-up and rehabilitation unit	6 (9.1)	19 (3.7)			
Nursing home	9 (13.6)	28 (5.4)	**.002**		
ADL					
<6	35 (53)	175(34.0)	**.002**		
6	30 (45.5)	339 (65.8)			
IADL					
<4	45 (68.2)	254 (49.3)	**.005**	1.60 (0.89–2.96)	.12
4	21 (31.8)	261 (50.7)		1	
MNA[b]					
<17	15 (22.7)	54 (10.5)			
17–23.5	30 (45.5)	210 (40.8)	**.0004**		
>23.5	16 (24.2)	231 (44.9)			
Malnutrition					
Yes	38 (57.6)	181 (35.1)	**.0003**		
No	26 (39.4)	331 (64.3)			
Hb					
≥10 g/dL	49 (74.2)	463 (89.9)			
<10 g/dL	17 (25.8)	51 (9.9)	**.0003**		
BCI					
>40,000	15 (22.7)	17 (3.3)	**<.0001**	5.12 (2.20–12.27)	**.0002**
≤40,000	50 (75.8)	494 (95.9)		1	
Albumin					
30–35 g/L	21 (31.8)	54 (10.4)	**<.0001**	1.71 (1.00–2.89)	**.05**
>35 g/L	43 (65.2)	451 (87.6)		1	

[a]Total percentages do not always reach 100% because of missing data.
[b]Metastatic stage: n = 554 patients; MNA: n = 589 patients. For all other variables, missing values <5%.
Abbreviations: ADL, activities of daily living; BCI, B12 × C-reactive protein index; CI, confidence interval; Hb, hemoglobin, IADL, instrumental activities of daily living; MNA, Mini Nutritional Assessment; OR, odds ratio.

before initiation of oncological treatment. Furthermore, reasons for unplanned hospitalization were not prospectively recorded. The geriatric population is very heterogeneous with a high median age (81 years); therefore, our study included various tumor sites and various tumor stages. Finally, comorbidities were not studied in our work, and liver diseases or renal failure could increase serum vitamin B12 levels.

The strengths of the study include data on unplanned hospitalizations at 1 and 3 months in older patients with cancer, which have been reported in very few studies in the oncology literature. This work included a large number of older ambulatory patients (621 persons). Serum vitamin B12 levels and BCI are not used in practice and could be easy and convenient in ambulatory and general medicine.

Conclusion

BCI (B12 × CRP) is prognostic factor of early death in older patients with cancer before initiation of oncological treatment. However, BCI is also a prognostic factor of unplanned and early hospitalizations in this same ambulatory population. In our work, other factors influenced unplanned hospitalizations at 1 month: IADL and albumin level. A future study to develop an early hospitalization score in older cancer adults in outpatient care would integrate IADL, albumin level, and BCI.

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Disclosures

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